§455.310d Chloramphenicol-polymyxin ointment.

(a) *Requirements for certification.* Chloramphenicol-polymyxin ointment conforms to all requirements and is subject to all procedures prescribed by §455.310c(a) for chloramphenicol ointment, except that:

(1) It contains not less than 10,000 units of polymyxin B per gram. The polymyxin B used conforms to the requirements prescribed for polymyxin B by §444.170a(a)(1) of this chapter.

(2) In lieu of the labeling prescribed by §455.310c(a)(3)(i)(*a*), each package shall bear on the outside wrapper or container and the immediate container, the statement ''Expiration date ————————'', the blank being filled in with the date that is 24 months after the month during which the batch was certified, except that the blank may be filled in with the date that is 36 months, 48 months, or 60 months after the month during which the batch was certified if the person who requests certification has submitted to the Commissioner results of tests and assays showing that after having been stored for such period of time such drug as prepared by him complies with the standards prescribed by this section: *Provided however,* That such expiration date may be omitted from the immediate container if it contains a single dose and it is packaged in an individual wrapper or container.

(3) In addition to complying with the requirements of §455.310c(a)(4), a person who requests certification of a batch shall submit with his request a statement showing the batch mark and (unless previously submitted) the results and date of the latest tests and assays of the polymyxin used in making the batch for potency. He shall also submit in connection with his request a sample consisting of not less than 6 packages of ointment and (unless it was previously submitted) a sample consisting of 5 packages containing approximately equal portions of not less than 0.5 gram each of the polymyxin used in making the batch.

(b) *Tests and methods of assay*—(1) *Potency*—(i) *Chloramphenicol content.* Proceed as directed in §455.310c(b). Its chloramphenicol content is satisfactory if it contains not less than 90 percent and not more than 120 percent of the number of milligrams per gram that it is represented to contain.

(ii) *Polymyxin content.* Proceed as directed in §444.170a(b)(2)(i) of this chapter, except in lieu of the directions in §444.170a(b)(2)(i)(*g*) of this chapter for the preparation of the sample, prepare the sample as follows: Place an accurately weighed sample (usually approximately 1.0 gram) in a separatory funnel containing approximately 50 milliliters of peroxide-free ether, and shake the sample and ether until homogeneous. Add 25 milliliters of 10-percent potassium phosphate buffer, pH 6.0 and shake. Remove the buffer layer and repeat the extraction with three additional 25-milliliter portions of buffer. Combine the extractives and make the proper estimated dilutions, using the buffer solution, except that, if the sample contains a water-soluble base, place an accurately weighed representative sample in a blending jar containing 1.0 milliliter of polysorbate 80 and sufficient 10 percent potassium phosphate buffer, pH 6.0, to give a final volume of 200 milliliters. Using a highspeed blender, blend the mixture for 2 minutes to 3 minutes and then make the proper estimated dilutions with 10 percent phosphate buffer pH 6.0. Its content of polymyxin is satisfactory if it contains not less than 90 percent and not more than 125 percent of the number of units per gram that it is represented to contain.

(2) *Sterility.* If the ointment is intended for ophthalmic use, proceed as directed in §436.20 of this chapter, using the method described in paragraph (e)(3) of that section. However, if the ointment is not soluble in isopropyl myristate proceed as directed in §436.20 of this chapter, using the method described in paragraph (e)(2) of that section, except use 100 milligrams in lieu of 300 milligrams of solids.

[39 FR 19166, May 30, 1974, as amended at 47 FR 23443, May 28, 1982; 50 FR 19921, May 13, 1985]

§455.310e Chloramphenicol - hydrocortisone acetate for ophthalmic suspension.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality,*

and purity. Chloramphenicol-hydrocortisone acetate for ophthalmic suspension contains 12.5 milligrams of chloramphenicol and 25 milligrams of hydrocortisone acetate with one or more suitable and harmless buffer substances, preservatives, and diluents. When reconstituted as directed in the labeling, its potency is not less than 90 percent and not more than 130 percent of the number of milligrams of chloramphenicol that it is represented to contain. It is sterile. Its pH is not less than 7.1 and not more than 7.5. The chloramphenicol used conforms to the standards prescribed by § 455.10(a)(1).

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(*a*) The chloramphenicol used in making the batch for potency, pH, specific rotation, melting range, absorptivity, and crystallinity.

(*b*) The batch for potency, sterility, and pH.

(ii) Samples required:

(*a*) The chloramphenicol used in making the batch: 10 packages, each containing approximately 300 milligrams.

(*b*) The batch:

(*1*) For all tests except sterility: A minimum of five immediate containers.

(*2*) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1) *Potency.* Use either of the following methods:

(i) *Microbiological turbidimetric assay.* Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Reconstitute as directed in the labeling. Dilute an accurately measured representative aliquot of the sample with sufficient distilled water to obtain a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with distilled water to the reference concentration of 2.5 micrograms of chloramphenicol per milliliter (estimated).

(ii) *Spectrophotometric assay.* Reconstitute the sample as directed in the labeling and dilute a 1.0-milliliter aliquot in sufficient distilled water to obtain a solution containing 20 micrograms of chloramphenicol per milliliter. Dissolve an accurately weighed portion of the working standard in sufficient distilled water to obtain a solution containing 20 micrograms per milliliter. Using a suitable spectrophotometer and distilled water as the blank, determine the absorbance of the sample and standard solutions at 278 nanometers. Calculate the potency of the sample as follows:

Milligrams of chloramphenicol per milliliter=Absorbance of sample X labeled potency per milliliter in milligrams/Absorbance of standard.

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

(3) *pH.* Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 5 milligrams per milliliter.

[49 FR 6093, Feb. 17, 1984]

§ 455.390 Vidarabine monohydrate ophthalmic ointment.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Vidarabine monohydrate ophthalmic ointment contains in each gram vidarabine monohydrate equivalent to 28.11 milligrams of vidarabine in a suitable and harmless base. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of vidarabine that it is represented to contain. It is sterile. It passes the test for metal particles. The vidarabine monohydrate used conforms to the standards prescribed by § 455.90a(a)(1).

(2) *Labeling.* In addition to the labeling requirements prescribed by § 432.5 of this chapter, this drug shall be labeled ''vidarabine ophthalmic ointment''.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:k